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EXAMINER	
ARCHIE, NINA	

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1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/526,369	KATSUYAMA ET AL.	
	Examiner	Art Unit	
	Nina A. Archie	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/31/2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5 and 7-28* is/are pending in the application.

4a) Of the above claim(s) *7-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,19-22,24,25 and 27* is/are rejected.

7)☒ Claim(s) *23,26 and 28* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This Office is responsive to Applicant's amendment and response filed 12-31-08. Claims 1-5, 7-28 are under examination. Claim 6 have been cancelled. Claims 7-18 are withdrawn. Claims 1-5 and 19-28 are pending.

Rejections Withdrawn

2. In view of the Applicant's amendment and remark following objections are withdrawn.

a) Rejection to claims 1 and 19 under 35 U.S.C. 112, first paragraph is withdrawn in light of applicant's amendment to the specification and applicant's argument.

b) Rejection to claims 1 and 19 under 35 U.S.C. 112, second paragraph is withdrawn in light of applicant's amendment to the specification and applicant's argument.

New Grounds of Rejections

Claim Rejections-35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written Description

3. Claims 21-22, 24-25, and 27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejected claims are drawn to a method of screening for a physiologically active substance, wherein the amino acid sequence of said protein comprises an amino acid sequence having a sequence identity of 90% or more to the amino acid sequence of

SEQ ID NO:1 (claims 21 and 22); wherein said protein is Tob family protein and or a Caf family protein, wherein the amino acid sequence of said protein comprises an amino acid having a sequence identity of 90 and 95% or more to the amino acid sequence of SEQ ID NO: 2, wherein the amino acid sequence of said protein comprises an amino acid having a sequence identity of 95% or more to the amino acid sequence of SEQ ID NO: 4 (claims 24-25 and 27).

The claims are drawn to a vast genus of amino acids of said protein comprising an amino acid having a sequence identity of 90 and 95% or more to the amino acid sequence of SEQ ID NO: 2, wherein the amino acid sequence of said protein comprises an amino acid having a sequence identity of 95% or more to the amino acid sequence of SEQ ID NO: 4 (claims 24-25 and 27) in a method of screening for a physiologically active substance.

To fulfill the written description requirements set forth under 35 USC § 112, first paragraph, the specification must describe at least a substantial number of the members of the claimed genus, or alternatively describe a representative member of the claimed genus, which shares a particularly defining feature common to at least a substantial number of the members of the claimed genus, which would enable the skilled artisan to immediately recognize and distinguish its members from others, so as to reasonably convey to the skilled artisan that applicant has possession the claimed invention. To adequately describe the genus of amino acids of said protein comprising an amino acid having a sequence identity of 90 and 95% or more to the amino acid sequence of SEQ ID NO: 2, wherein the amino acid sequence of said protein comprises an amino acid having a sequence identity of 95% or more to the amino acid sequence of SEQ ID NO: 4 (claims 24-25 and 27), applicant must also give a functional limitation in a method of screening for a physiologically active substance.

Applicants have only disclosed the following. Applicants disclose proteins belonging to Caf family and Tob Family (see pgs. 14-19). Said description indicated does not correlate to the claimed functions set forth in the instant claims. Applicant has not demonstrated that any in a method of screening for a physiologically active substance, wherein the amino acids of said protein comprising an amino acid having a sequence

identity of 90 and 95% or more to the amino acid sequence of SEQ ID NO: 2, wherein the amino acid sequence of said protein comprises an amino acid having a sequence identity of 95% or more to the amino acid sequence of SEQ ID NO: 4 (claims 24-25 and 27). Furthermore Applicants have not disclosed variants of the above method, capable of the directed claims (claims 21-22, 24-25, and 27). The specification further does not disclose distinguishing and identifying features of a representative number of members of the genus of immunogenic compositions to which the claims are drawn, such as a correlation between the structure of the amino acids of said protein comprising an amino acid having a sequence identity of 90 and 95% or more to the amino acid sequence of SEQ ID NO: 2, wherein the amino acid sequence of said protein comprises an amino acid having a sequence identity of 95% or more to the amino acid sequence of SEQ ID NO: 4 (claims 24-25 and 27) and the method of screening for a physiologically active substance so that the skilled artisan could immediately envision, or recognize at least a substantial number of members of the claimed genus as set forth supra (claims 21-22, 24-25, and 27). Moreover, the specification fails to disclose which amino acid residues are essential to the function of the protein or which amino acids might be replaced or by which other amino acids the essential amino acids might be replaced so that the resultant protein retains the activity of its parent. Therefore, since the specification fails to adequately describe at least a substantial number of members of the genus as set forth supra to which the claims are based; the specification fails to adequately describe at least a substantial number of members of the claimed genus of amino acids of said protein comprising an amino acid having a sequence identity of 90 and 95% or more to the amino acid sequence of SEQ ID NO: 2, wherein the amino acid sequence of said protein comprises an amino acid having a sequence identity of 95% or more to the amino acid sequence of SEQ ID NO: 4 (claims 24-25 and 27) in a method of screening for a physiologically active substance.

MPEP § 2163.02 states, "[a]n objective standard for determining compliance with the written description requirement is, 'does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed' ". The courts have decided: The purpose of the "written description" requirement is broader than to

merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the "written description" inquiry, whatever is now claimed. See Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Federal Circuit, 1991). Furthermore, the written description provision of 35 USC § 112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiefs v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. 1I. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, "'Written Description" Requirement (66 FR 1099-1111, January 5, 2001) state, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (Id. at 1104). Moreover, because the claims encompass a genus of variant species, an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that Applicant was in possession of the claimed genus. However, factual evidence of an actual reduction to practice has not been disclosed by Applicant in the specification; nor has Applicant shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete; nor has Applicant described distinguishing identifying characteristics sufficient to show that Applicant were in possession of the claimed invention at the time the application was filed. The Guidelines further state, "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus" (Id. at 1106); accordingly, it follows that an adequate written

description of a genus cannot be achieved in the absence of a disclosure of at least one species within the genus. Absent factual evidence, a percentage sequence similarity of less than 100 % is not deemed to reasonably support to one skilled in the art whether the biochemical activity of the claimed subject matter would be the same as that of a similar known biomolecule. It is known for nucleic acids as well as proteins, for example, that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. The effects of these changes are largely unpredictable as to which ones have a significant effect versus not. Therefore, the citation of sequence similarity results in an unpredictable and therefore unreliable correspondence between the claimed biomolecule and the indicated similar biomolecule of known function and therefore lacks support regarding utility and/or enablement.

Therefore, because the art is unpredictable, in accordance with the Guidelines, the description of amino acids of said protein comprising an amino acid having a sequence identity of 90 and 95% or more to the amino acid sequence of SEQ ID NO: 2, wherein the amino acid sequence of said protein comprises an amino acid having a sequence identity of 95% or more to the amino acid sequence of SEQ ID NO: 4 (claims 24-25 and 27) is not deemed representative of the genus of as set forth supra to which the claims refer. Hence, none of the claims meet the written description requirements.

Enablement

4. Claims 21-22, 24-25, and 27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contain subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification is not enabled for method of screening for a physiologically active substance, wherein the amino acid sequence of said protein comprises an amino acid sequence having a sequence identity of 90% or more to the amino acid sequence of SEQ ID NO:1 (claims 21 and 22); wherein said protein is Tob family protein and or a Caf family protein, wherein the amino acid sequence of said protein comprises an amino acid

having a sequence identity of 90 and 95% or more to the amino acid sequence of SEQ ID NO: 2, wherein the amino acid sequence of said protein comprises an amino acid having a sequence identity of 95% or more to the amino acid sequence of SEQ ID NO: 4 (claims 24-25 and 27).

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary.

In re Fisher, 427 F.2d 833,839, 166 USPQ 18, 24 (CCPA 1970) states, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." "The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling" (MPEP 2164.03). The MPEP further states that physiological activity can be considered inherently unpredictable. Thus, Applicant assumes a certain burden in establishing that inventions involving physiological activity are enabled. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the invention:

The instant claims are drawn to method of screening for a physiologically active substance, wherein the amino acid sequence of said protein comprises an amino acid sequence having a sequence identity of 90% or more to the amino acid sequence of SEQ ID NO:1 (claims 21 and 22); wherein said protein is Tob family protein and or a Caf family protein, wherein the amino acid sequence of said protein comprises an amino acid having a sequence identity of 90 and 95% or more to the amino acid sequence of SEQ ID

NO: 2, wherein the amino acid sequence of said protein comprises an amino acid having a sequence identity of 95% or more to the amino acid sequence of SEQ ID NO: 4 (claims 21-22, 24-25, and 27).

Breadth of the claims:

A method of screening a physiologically active substance is overly broad. Furthermore the product being used to screen a physiologically active substance, comprising a) contacting a test sample with a transformed yeast capable of expressing a protein involved in proliferation or differentiation of cells or regulating cell cycles of a mammalian cell, wherein the transformed yeast is respiration ability deficient and show is capable of expressing a heterogeneous protein (claim 1);

or

a) culturing a test culture comprising a test physiologically active substance and a yeast transformed with a recombinant expression vector, wherein said transformed yeast is respiration deficient and has a sensitized growth rate due to the expression of a heterogeneous protein encoded by said vector, and wherein said protein controls the proliferation of mammalian cells or regulates the cell cycle of mammalian cells (claim 19);

wherein the amino acid sequence of said protein comprises an amino acid sequence having a sequence identity of 90% or more to the amino acid sequence of SEQ ID NO:1 (claims 21 and 22); wherein said protein is Tob family protein and or a Caf family protein, wherein the amino acid sequence of said protein comprises an amino acid having a sequence identity of 90 and 95% or more to the amino acid sequence of SEQ ID NO: 2, wherein the amino acid sequence of said protein comprises an amino acid having a sequence identity of 95% or more to the amino acid sequence of SEQ ID NO: 4 (claims 24-25 and 27) is overly broad. Therefore it hard for one skilled in the art to determine if the protein and it recited function in the instant claims can be used in a method of screening a physiologically active substance.

Guidance of the specification/The existence of working examples:

Applicants disclose expression of hcaf, tob proteins and lckYf genes and growth experiments (see 55-79). Applicants disclose proteins consisting of the amino acid sequences shown in SEQ ID NO: 1, 2, and 4 comprising an amino acid sequence having a sequence identity of preferably 90% or most preferably 95% (see pg. 15-16). The data indicated aforementioned above is not indicative of the method as claimed (claims 21-22, 24-25, and 27). However, the specification does not disclose any variants of the amino acids in instant claims that are capable of lowering in the growth of a yeast in the expression state thereof. The data presented in the specification is not indicative and merely contemplated of the directed claims (21-22, 24-25, and 27).

State of the art:

While the skill in the art of immunology is high, to date, prediction of a specific immune response for any given composition in any given animal is quite unpredictable. Moreover, protein chemistry is probably one of the most unpredictable areas of biotechnology. Consequently, the effects of sequence dissimilarities upon protein structure and function cannot be predicted. Bowie et al. (Science, 1990, 247:1306-1310) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function, carry out the instructions of the genome and form immunoepitopes. Bowie et al. further teach that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. (column 1, page 1306). Bowie et al. further teach that while it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (column 2, page 1306).

Consequently, in view of the lack of support in the art and specification, it would require undue experimentation on the part of the skilled artisan to make and use the composition as claimed; therefore, the full scope of the claims is not enabled.

Claim Rejections-35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1 and 19, and all dependent claims 2-5 and 20-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

As to Claims 1, and all dependent claims 2-5 recites the limitation "cultured". As to claims 19, and all dependent claims 20-28, a dependent claim, recites the limitation "protein" and "vector". There is insufficient antecedent basis for these limitations in the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -
(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore,

the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

6. Claims 1-3 and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Meier et al US Application 2005/0118576 Date June 2, 2005 Filing Date July 11, 2001.

The claims are drawn to a method of screening a physiologically active substance, comprising the steps of: a) contacting a test sample with a transformed yeast; capable of expressing a protein involved in proliferation or differentiation of cells or regulating cell cycles of a mammalian cell, wherein the transformed yeast is respiration ability deficient and show a change in the growth rate of said transformed yeast; b) culturing said transformed yeast under conditions that result in expression of said protein and c) measuring the growth rate of said cultured yeast, wherein the physiologically active substance is judged to be present in the test sample in a case where the growth of the yeast is lowered or improved in the presence of the test sample as compared to that in the absence of the test sample as a control (claim 1).

Meier et al teach a method wherein yeast mutants deficient in the expression of the yeast homolog of frataxin are applied for the identification and/or evaluation of pharmaceutically active compounds (see abstract). Meier et al teach cell-based in screening assays for the identification and validation of novel drug candidates with special emphasis on yeast-based screening procedures for pharmaceutically active chemical and biochemical compounds (See 0001). Meier et al teach a yeast strain in which the gene encoding the "yeast homolog of frataxin" is disrupted. Frataxin is a nuclear encoded protein involved in the regulation of iron homeostasis of mitochondria as for example in yeast, animals and human tissue (see 0002) which correlates to a method of screening a physiologically active substance, comprising the steps of: a) contacting a test sample with a transformed yeast; capable of expressing a protein involved in proliferation or differentiation of cells or regulating cell cycles of a mammalian cell (claim 1). Meier et al teach increased frequency in the partial or complete loss of mitochondrial DNA leading to the formation of so called rho.sup.- mutants (respiration deficient mutants) which are unable to perform oxidative phosphorylation (see 0006). Meier et al teach reduced growth rates when cultured in medium containing non-fermentable carbon sources; (see 0007); Meier et al teach shows the growth of wild-type

W303-1B and mutant yeast in the presence of CuSO.sub.4 (test sample) as determined by OD.sub.620 measurement and increasing concentrations of CuSO.sub.4 clearly inhibit the growth of the frataxin deficient yeast (see 0025) which correlates to the transformed yeast is respiration ability deficient and show a change in the growth rate of said transformed yeast; b) culturing said transformed yeast under conditions that result in expression of said protein and c) measuring the growth rate of said cultured yeast, wherein the physiologically active substance is judged to be present in the test sample in a case where the growth of the yeast is lowered or improved in the presence of the test sample as compared to that in the absence of the test sample as a control (claim 1). Meier et al teach a method wherein expression of said protein causes lowering growth rate of said transformed yeast as compared to a culture of said transformed yeast that is not expressing said protein (see Figure 2B and pg. 4) (claim 2), wherein said protein (Frataxin) involved in regulating cell cycle of a mammal cell(see 0001) (claim 3), wherein the growth rate said transformed yeast is determined by change in endogenous enzyme activity (see 0008) (claim 5).

Claim Rejections - 35 USC § 103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1-5, 19-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Meier et al US Application 2005/0118576 Date June 2, 2005 Filing Date July 11, 2001 in view of Bounaga et al WO 01/20020 March 23, 2001, and Naihe et al WO 02/68687 September 6, 2002 as evidenced by Nakahama et al January 26, 1993 US Patent No. 5182195.

The claims are drawn to

A method of screening a physiologically active substance, comprising the steps of: a) contacting a test sample with a transformed yeast; capable of expressing a protein involved in proliferation or differentiation of cells or regulating cell cycles of a mammalian cell, wherein the transformed yeast is respiration ability deficient and show a change in the growth rate of said transformed yeast; b) culturing said transformed yeast under conditions that result in expression of said protein and c) measuring the growth rate of said cultured yeast, wherein the physiologically active substance is judged to be present in the test sample in a case where the growth of the yeast is lowered or improved in the presence of the test sample as compared to that in the absence of the test sample as a control (claim 1);

A method of screening for a physiologically active substance, comprising:
(a) culturing a test culture comprising a test physiologically active substance and a yeast transformed with a recombinant expression vector, wherein said transformed yeast is respiration deficient and has a sensitized growth rate due to the expression of a heterogeneous protein encoded by said vector, and wherein said protein controls the proliferation of mammalian cells or regulates the cell cycle of mammalian cells;
(b) measuring a growth state of said transformed yeast in said test culture;
(c) culturing a control culture of said transformed yeast;
(d) measuring a growth state of said control culture; and
(e) comparing the growth states of said test and control cultures; wherein said test physiologically active substance is judged to have physiological activity where the growth state of said transformed yeast in said test culture is lowered or improved as compared to the growth rate of said yeast in said control culture (claim 19), wherein said protein is a Tob family protein and or a Caf family protein (claim 20).

Meier et al teach a method wherein yeast mutants deficient in the expression of the yeast homolog of frataxin are applied for the identification and/or evaluation of pharmaceutically active compounds (see abstract). Meier et al teach cell-

based in screening assays for the identification and validation of novel drug candidates with special emphasis on yeast-based screening procedures for pharmaceutically active chemical and biochemical compounds (See 0001). Meier et al teach a yeast strain in which the gene encoding the "yeast homolog of frataxin" is disrupted. Frataxin is a nuclear encoded protein involved in the regulation of iron homeostasis of mitochondria as for example in yeast, animals and human tissue (see 0002) which correlates to a method of screening a physiologically active substance, comprising the steps of: a) contacting a test sample with a transformed yeast; capable of expressing a protein involved in proliferation or differentiation of cells or regulating cell cycles of a mammalian cell (claim 1). Meier et al teach increased frequency in the partial or complete loss of mitochondrial DNA leading to the formation of so called rho.sup.- mutants (respiration deficient mutants) which are unable to perform oxidative phosphorylation (see 0006). Meier et al teach reduced growth rates when cultured in medium containing non-fermentable carbon sources; (see 0007); Meier et al teach shows the growth of wild-type W303-1B and mutant yeast in the presence of CuSO.sub.4 (test sample) as determined by OD.sub.620 measurement and increasing concentrations of CuSO.sub.4 clearly inhibit the growth of the frataxin deficient yeast (see 0025) which correlates to the transformed yeast is respiration ability deficient and show a change in the growth rate of said transformed yeast; b) culturing said transformed yeast under conditions that result in expression of said protein and c) measuring the growth rate of said cultured yeast, wherein the physiologically active substance is judged to be present in the test sample in a case where the growth of the yeast is lowered or improved in the presence of the test sample as compared to that in the absence of the test sample as a control (claim 1). Meier et al teach a method wherein expression of said protein causes lowering growth rate of said transformed yeast as compared to a culture of said transformed yeast that is not expressing said protein (see Figure 2B and pg. 4) (claim 2), wherein said protein (Frataxin) involved in regulating cell cycle of a mammal cell(see 0001) (claim 3), wherein the growth rate said transformed yeast is determined by change in endogenous enzyme activity (see 0008) (claim 5).

Meier et al is relied upon as set forth supra. However Meier et al does not teach a method, wherein protein involved in intracellular signaling of G0/G1 phase of a mammal cell (claim 4). Meier el al does not teach a method comprising a yeast transformed with a recombinant expression vector (claim 19), wherein said protein is a Tob family protein and or a Caf family protein (claim 20).

Bounaga et al teach a method for screening and identification of compounds or compositions comprising (1) addition of a compound or composition to be screened or identified to a culture or culture area of a yeast strain transformed with and expressing one or more plant or animal or human cell cycle control genes or mutants thereof as well as to a control yeast strain; and (2) determining the effect on the phenotype such as inhibition or stimulation of growth and/or cell division and/or changing cell shape and size of said transformed yeast compared to said control yeast (page 4 lines 1-9, page 7 line 21, page 12 lines 30-34). Bounaga et al teach that the transformed yeast expresses a cell cycle control gene resulting in growth arrest or growth acceleration (page 30 claims 7 and 8) and said cell cycle control gene is involved in regulation of cell cycle of a mammal (page 12 lines 30-34), for example, involved in control of entry (that is from GO/G1 phase) and progression through S phase of the cell cycle (page 5 lines 9-10) such as cyclin dependent kinases (CDK), cyclin dependent kinase inhibitor, cyclin A, D, E etc (page 5 line 1-9 and lines 10-34 and page 6 lines 1-9) (claim 4). Bounaga et al teach that the present invention includes the use of a recombinant vector comprising at least one polynucleic acid encoding at least part of a plant cell cycle control protein or a mutant thereof to transform yeast for the screening or identification of compounds or compositions which abolish, retard or stimulate plant growth. Said recombinant vector is a plasmid, more particularly a vector comprising a selectable marker and transcriptional control elements for the expression of said plant or animal/human cell cycle control polynucleic acids in yeast. Said plant or animal/human cell cycle control polynucleic acid is integrated into the yeast genome by random, non-homologous or homologous recombination (see pg. 13 lines 1-10) (claim 19).

Naihe et al teach wherein a protein is Tob family protein. Naihe et al teach that Tob protein manifest an inhibiting action on cell growth thus Naihe et al teach a protein that controls cell proliferation (see pg. 1 paragraph 3) (claim 20).

It would have been prima facie obvious at the time the invention was made to modify the method of Meier et al. by incorporating a protein involved in intracellular signaling of G0/G1 phase of a mammal cell as set forth supra as taught by Bounaga et al in order to take advantage regulating cell cycles of a mammalian cell.

One would have a reasonable expectation of success because to use protein involved in intracellular signaling of G0/G1 phase of a mammal in the method (as disclosed Bounaga et al) is well known in the art.

It would have been prima facie obvious at the time the invention was made to modify the method of Meier et al. by incorporating a protein is Tob family protein as set forth supra as taught by Naihe et al in order to take advantage of Tob protein manifesting an inhibiting action on cell growth thus Naihe et al teach a protein that controls cell proliferation.

One would have a reasonable expectation of success because to use protein involved controls cell proliferation (as disclosed Naihe et al) is well known in the art.

Status of the Claims

9. No claims are allowed.

Claims 1-5, 19-22, 24-25, and 27 are rejected.

Claims 23, 26, and 28 are objected as being dependent on a rejected on base claim.

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nina A. Archie whose telephone number is 571-272-9938. The examiner can normally be reached on Monday-Friday 8:30-5:00p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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